



[Billing Code 4140-01-P]

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health (NIH)

Office of Science Policy, Office of Biotechnology Activities; Recombinant or Synthetic

Nucleic Acid Molecule Research: Action Under the NIH Guidelines for Research

Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)

AGENCY: NIH, Public Health Service, HHS.

ACTION: Notice of Final Action under the NIH Guidelines.

SUMMARY: The Office of Biotechnology Activities (OBA) is updating Appendix B (Classification of Human Etiologic Agents on the Basis of Hazard) of the NIH Guidelines by specifying the risk group (RG) classification for two organisms: Middle East Respiratory Syndrome coronavirus (MERS-CoV) and Pseudomonas aeruginosa.

BACKGROUND: The NIH Guidelines provide guidance to investigators and local Institutional Biosafety Committees (IBCs) for setting containment for research involving recombinant or synthetic nucleic acid molecules. Section II-A, Risk Assessment, instructs investigators and IBCs to make an initial risk assessment based on the RG of the

agent that will be manipulated (see Appendix B, Classification of Human Etiologic Agents on the Basis of Hazard). The RG of the agent often correlates with the minimum containment level required for experiments subject to the NIH Guidelines. Updating Appendix B by revising the risk groups for certain organisms, or adding new organisms, leads to more uniform containment recommendations that are commensurate with the biosafety risk.

The resulting amendments are “Minor Actions” under Section IV-C-1-(b)-2 of the NIH Guidelines and, therefore, will be implemented immediately upon publication in the Federal Register. However, the OBA welcomes public comment to inform any future changes to Appendix B.

DATES: Comments may be submitted to the OBA in paper or electronic form at the mailing, fax, and e-mail addresses shown below under the heading “For Further Information.” All comments should be submitted by [Insert date 30 days after date of publication in the Federal Register]. All written comments received in response to this notice will be available for public inspection in the NIH OBA office, 6705 Rockledge Drive, Suite 750, MSC 7985, Bethesda, MD 20892-7985, weekdays between the hours of 8:30 a.m. and 5:00 p.m.

FOR FURTHER INFORMATION: If you have questions, or require additional information about these changes, please contact the OBA by e-mail at [oba@od.nih.gov](mailto:oba@od.nih.gov) or by telephone at 301-496-9838. Comments may be submitted to the same e-mail address

or by fax to 301-496-9839 or by mail to the Office of Biotechnology Activities, National Institutes of Health, 6705 Rockledge Drive, Suite 750, Bethesda, Maryland 20892-7985. Background information may be obtained by contacting the NIH OBA by e-mail at [oba@od.nih.gov](mailto:oba@od.nih.gov).

### Middle East Respiratory Syndrome coronavirus (MERS-CoV)

MERS-CoV is an emerging infectious disease agent that was originally identified in 2012 in Saudi Arabia. The virus is a member of the order Nidovirales, family Coronaviridae, and causes a severe pulmonary syndrome that is similar to what was seen with Severe Acute Respiratory Syndrome coronavirus (SARS-CoV). MERS-CoV has been identified as the cause of a severe respiratory disease in 144 individuals, of which 62 have died (as of October 25, 2013; source: Centers for Disease Control and Prevention (CDC) -- <http://www.cdc.gov/coronavirus/mers/>). The overall mortality rate of MERS-CoV infection to date is about four times higher than what was reported for SARS-CoV; although it is of note, in patients over 65 years of age, that mortality from infection with SARS-CoV was reported to exceed 50 percent (based on World Health Organization (WHO) data accessed September 9, 2013, [http://www.who.int/csr/sars/archive/2003\\_05\\_07a/en/print.html](http://www.who.int/csr/sars/archive/2003_05_07a/en/print.html)). As was the case for SARS-CoV, there are no proven preventive or therapeutic measures against this new virus. In addition, there are many unanswered questions regarding this virus, including questions about how the virus is transmitted. Although the incidence of viral infections caused by MERS-CoV remains highest in, and largely localized to the Arabian Peninsula

(138 of 144 cases), the high mortality rate associated with this agent and its epidemic potential has led to close monitoring by the WHO

([http://www.who.int/csr/disease/coronavirus\\_infections/faq/en/index.html](http://www.who.int/csr/disease/coronavirus_infections/faq/en/index.html)).

Under Appendix B of the NIH Guidelines, most coronaviruses are classified as RG2 viruses. Given the severity of illness seen to date, MERS-CoV will be added to the list of RG3 agents, as was done for SARS-CoV. However, because little is currently known about the source, reservoir, and epidemiology of this virus, the RG classification will be reassessed if new data emerge relevant to the biosafety risks associated with the agent. In addition, while research with RG3 agents is often carried out at Biosafety level 3 containment—with appropriate enhancements depending upon the nature of the agent, e.g., increased respiratory precautions for agents that are transmissible by the aerosol route—the RG of an agent is not the only factor that determines the containment level. As stated in Section II-A of the NIH Guidelines (Risk Assessment) “once the risk group of an agent is identified, this should be followed by a thorough consideration of how the agent is to be manipulated” and there may be experiments for which a higher containment level is warranted. Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with MERS-CoV are available on the CDC website at the following URL: <http://www.cdc.gov/coronavirus/mers/guidelines-lab-biosafety.html>.

Pseudomonas aeruginosa

Bacteria belonging to the genus Pseudomonas are ubiquitous in the environment. They are generally considered to be opportunistic pathogens, i.e., able to cause disease in individuals who are immunocompromised. According to the CDC, serious pseudomonas infections usually occur in hospitalized patients and those who are immunocompromised and these infections can lead to severe illness and death (<http://www.cdc.gov/hai/organisms/pseudomonas.html>). Healthy people can also become ill from Pseudomonas aeruginosa, especially after exposure to inadequately disinfected water. Per the CDC, “Ear infections, especially in children, and more generalized skin rashes may occur after exposure to inadequately chlorinated hot tubs or swimming pools. Eye infections have occasionally been reported in persons using extended-wear contact lenses” (<http://www.cdc.gov/hai/organisms/pseudomonas.html>).

Because this bacterium generally causes mild disease in healthy individuals and there are antibiotics to treat such disease, the OBA will add it to Appendix B as an RG2 bacterium. This is consistent with other assessments of the RG for this pathogen by other biosafety guidances, including the Canadian (<http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/pseudomonas-spp-eng.php>) and the European Community (<http://www.bacterio.net/hazard.html#group2>) guidances.

Appendix B-II-A. Risk Group 2 (RG2) - Bacterial Agents Including Chlamydia.

The following addition will be made to Appendix B-II-A. Risk Group 2 (RG2) – Bacterial Agents Including Chlamydia:

Pseudomonas aeruginosa

The following addition will be made to Appendix B-III-D Risk Group 3 (RG3) - Viruses and Prions:

Middle East Respiratory Syndrome coronavirus (MERS-CoV)

Dated: October 30, 2013.

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[FR Doc. 2013-26612 Filed 11/05/2013 at 8:45 am; Publication Date: 11/06/2013]